The Exposure of Nonsmoking and Smoking Mothers to Environmental Tobacco Smoke during Different Gestational Phases and Fetal Growth

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We studied the impact of maternal exposure to environmental tobacco smoke (ETS) on birth weight (BW), low birth weight (LBW), and intrauterine growth retardation (IUGR) according to self-reported maternal smoking habits in a sample of 6,866 singleton births. We obtained data about parental characteristics and maternal active smoking (AS) and passive smoking at delivery via maternal questionnaires and medical records. We used three categories of smoking habits (nonsmokers and those who smoked 1–10 or >10 cigarettes per day) and defined ETS exposure as ≥ 5 cigarettes per day smoked by others in the mother's presence. We used multiple regression and logistic regression procedures with adjustment for many associated covariates. We observed a significant reduction of the mean BW in infants of AS mothers. This reduction was only marginal for mothers who stopped smoking after recognizing their pregnancy. ETS exposure in 1,797 of 5,507 nonsmoking mothers reduced the mean BW of their infants by 53 g [95% confidence interval (CI), 24–82 g]. ETS exposure also significantly reduced BW in babies of AS mothers by 92 g (CI, 21–113 g) compared with BW of ETS-nonexposed AS mothers. The adjusted odds ratio (AOR) of LBW for ETS-exposed AS mothers was two times the LBW risk of ETS-nonexposed AS mothers(2.02; CI, 1.11–3.67); the AOR of ETS-exposed nonsmoking mothers was 1.51 (CI, 1.02–2.26). The AOR of IUGR for this group did not differ from unity (1.08; CI, 0.82–1.43). However, ETS exposure increased the AOR of IUGR for AS mothers from 1.64 (CI, 1.06–2.53) to 2.13 (CI, 1.70–2.67). ETS exposure reduced the BW of infants of nonsmoking mothers and contributed to additional BW reduction in infants of AS mothers. ETS exposure increased the risk of LBW but not that of IUGR in babies of nonsmoking mothers. ***Key words:*** **active smoking, birth weight, environmental tobacco smoke, fetal growth, IUGR, low birth weight, passive smoking.** ***Environ Health Perspect*** **110:601–606 (2002). [Online 26 April 2002]**
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The exposure to environmental tobacco smoke (ETS), frequently referred to as passive smoking, is causally associated with a variety of health outcomes in nonsmokers (*1–3*). This applies not only to cardiovascular and respiratory illnesses, including lung cancer, but also to some adverse reproductive effects (*4–7*). Those most at risk from ETS exposure appear to be neonates, young children, and possibly the fetus (*8*). Study after study is finding that ETS exposure adversely affects fetal growth with an elevated risk of low birth weight (LBW) (*9–13*). The impact of passive smoking on other reproductive outcomes is less clear; an elevated risk of spontaneous abortion (*14*) and sudden infant death syndrome (*15*) as well as impaired female and male fertility (*16,17*) have been observed in some epidemiologic studies.

ETS—a complex mixture containing many developmental toxicants (e.g., polycyclic aromatic hydrocarbons, lead, nicotine, cadmium)—is an important source of indoor air contaminants. Alone, each smoker is exposed to self-produced ETS; smokers tend to spend more time in a smoking milieu being exposed to ETS produced by others. This additional exposure may increase the adverse effects of active smoking.

We examined the influence of self-reported active and passive smoking on fetal growth in a retrospective epidemiologic study in the frame of a wider project named the Teplice Program (*18*). The design of the present study enabled us to evaluate the effects of ETS on the fetal growth of infants delivered by nonsmoking mothers as well as by mothers who smoked during the different gestational phases (AS mothers).

Materials and Methods

We designed the study as a retrospective population study with an interview at delivery. The background sample included all singleton live births occurring in the districts of Teplice and Prachatice (Czech Republic) from April 1994 through March 1999. We excluded mothers who gave incomplete information about smoking and restricted the sample to the mother's first delivery in the study period. We obtained data about parental social, lifestyle, health and reproductive characteristics, and maternal active and passive smoking during early and later phases of pregnancy at delivery via self-administered maternal questionnaires and medical records [see Dejmek et al. (*19*) for more details]. The questionnaire data included information on maternal smoking habits during four periods: at the time when the index pregnancy was recognized and during the first, second, and third trimesters. We used three categories of smoking habits: nonsmokers, moderate smokers [smokers who admitted 1–10 cigarettes per day (cig/day)], and heavy smokers (admitted > 10 cig/day). On the basis of the results of a pilot study, we defined ETS as ≥ 5 cig/day that were smoked by others in the mother's presence (for more details, see "Discussion"). We also limited ETS exposure of AS mothers to exposure to the smoke of another persons (≥ 5 cig/day). We evaluated six exposure groups that combined maternal ETS and AS exposure. We used the number of cigarettes smoked per day in regression analyses.

We used birth weight (BW), LBW (BW < 2,500 g), and intrauterine growth retardation (IUGR; BW < 10th percentile of BW distribution for gestational week and sex) as reproductive outcome measures. We analyzed the relationship between BW and maternal smoking and/or ETS exposure using multiple regression methods and the association of adverse outcomes with maternal smoking and/or ETS using logistic regression procedures. We controlled for the influence of many potential confounding covariates or surrogates in regression models: maternal age, height, prepregnancy weight, parity, marital status, maternal alcohol

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consumption, education of parents, reproductive history, infant's sex, and season.

Results

We enrolled 6,866 mother–infant pairs in the sample, including 4,309 pairs (63%) in which the mother declared herself to be a nonsmoker during early gestation. Some mothers stopped smoking during pregnancy, and the proportion of nonsmoking mothers increased to 74% during the first trimester and to 80% during the second trimester. About 25% of nonsmoking mothers admitted an exposure to ETS, compared with 67% of the mild and 85% of the heavy AS mothers. Also, the reported daily number of cigarettes that were smoked by others in the mother's presence differed considerably according to smoking habits, increasing from 11 in nonsmoking mothers to 14 in moderate and to 23 in heavy AS mothers.

BW distribution. The results of multiple regression analysis showed a strong association between BW and maternal smoking habits (Table 1). This association tended to increase depending on the extent of smoking and the duration of smoking during pregnancy. This last tendency followed *indirectly* from a comparison of the results based on maternal smoking habits during the different periods of gestation. The association of BW with maternal smoking was weaker when we used data about smoking during early pregnancy, stronger with data characterizing smoking habits in the first trimester, and even stronger if based on smoking in the second and third trimester (Table 1).

To compare directly the impact of maternal smoking before pregnancy (and during early gestation) on BW with that of smoking during later gestational phases, we analyzed separately the sample of mothers who stopped smoking after they recognized their pregnancy. Regrettably, this restriction created a substantial reduction of the sample size and a corresponding decrease in the power of analysis: Only 754 (30%) of 2,549 mothers who were smoking before pregnancy gave up smoking after recognition of pregnancy. The relationship between smoking and BW in this maternal group was relatively weak and nonsignificant. The adjusted difference of the mean BW was –22 g [95% confidence interval (CI), ≥ 19 to –64 g] for moderate and 66 g (CI, ≥ 14 to –146 g) for heavy AS mothers. In contrast, the adjusted weight reduction for infants of mothers who continued smoking during the second trimester was –152 g (CI, –117 to –185 g) in moderate and –259 g (CI, –175 to –342 g) in heavy AS mothers. The BW reduction based on data about smoking in the third trimester was of very similar size (Table 1).

Multiple regression analysis showed a relationship between the BW of infants delivered by nonsmoking mothers and ETS exposure. The crude relation was highly significant with an average BW reduction of 89 g (CI, 53–124 g). After an adjustment for other covariates, the decrement was reduced to 53 g (CI, 24–82 g; Table 2).

A simultaneous exposure to ETS further reduced the BW in babies of AS mothers. This additional effect was relatively strong: the decrements for ETS-nonexposed versus ETS-exposed AS mothers were 119 g (CI, 48–190 g) and 192 g (CI, 155–228 g), respectively. We also estimated the impact of the combined active and/or passive smoking on BW separately for moderate and heavy AS mothers. This impact was again rather weak for the group of mothers who stopped smoking during early gestation. In fact, we observed a significant effect on BW only in ETS exposure alone (–41 g; CI, –5 to –77 g) and in moderate (–69 g; CI, –4 to –134 g) and heavy AS mothers (–88 g; CI, –17 to –159 g) who were simultaneously exposed to ETS (Figure 1, Table 3). This contrasts with the strong combined effects of smoking during pregnancy. The mean BW reduction in babies of AS mothers who smoked 1–10 cig/day during the second trimester was 181 g (CI, 148–226 g); this decrement was 271 g (CI, 183–358 g) for infants of ETS-exposed AS mothers who smoked >10 cig/day.

We did a direct statistical evaluation of the additional effect of ETS in AS mothers comparing the BW of infants born to AS mothers with and without passive smoking. Adjusted reduction of BW in infants of AS mothers who are exposed to ETS was 92 g (CI, 21–113 g) compared with ETS-nonexposed AS mothers.

Analyzing data about ETS exposure and smoking habits during different phases of pregnancy and their relation to BW, we obtained an interesting scale (Figure 2). The estimated effects increase from the weakest estimates for smoking before pregnancy to the strongest estimates based on data from the second trimester. We also found quite similar results by analyzing data about smoking during the third trimester. However, the numbers in some groups were too small to give

Table 1. BW by maternal smoking habits during different gestational phases (regardless of ETS exposure).

Maternal smoking	No.	BW (g)	Decrement (g) Crude	Adjusted[a]	95% CI	*p*-Value
Before pregnancy						
Nonsmoker	4,309	3,358 ± 498	0	0	—	—
Moderate[b]	1,500	3,233 ± 499	–125	–58	–29 to –88	0.0002
Heavy[c]	1,049	3,316 ± 533	–222	–136	–111 to –172	0.0052
First trimester						
Nonsmoker	5,043	3,350 ± 498	0	0	—	—
Moderate	1,522	3,167 ± 512	–183	–96	–66 to –127	0.0000
Heavy	293	3,046 ± 540	–304	–202	–139 to –265	0.0000
Second trimester						
Nonsmoker	5,510	3,347 ± 501	0	0	—	—
Moderate	1,180	3,112 ± 499	–235	–152	–117 to –185	0.0000
Heavy	176	2,943 ± 484	–404	–259	–175 to –342	0.0000
Third trimester						
Nonsmoker	5,562	3,348 ± 502	0	0	—	—
Moderate	1,035	3,119 ± 505	–229	–130	–95 to –166	0.0000
Heavy	170	2,940 ± 486	–408	–239	–154 to –323	0.0000

[a]Adjusted for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, prepregnancy weight, alcohol consumption, and season. [b]Moderate, 1–10 cig/day. [c]Heavy, > 10 cig/day.

Table 2. The impact of ETS exposure on birth outcomes of nonsmoking and AS mothers.

AS	ETS[b]	BW decrement[a] (95% CI)	AOR[a] (95% CI)
BW			
Nonsmoker	Exposed	53 g (24–82)	—
Smoker	—	119 g (48–190)	—
Smoker	Exposed	192 g (155–228)	—
LBW			
Nonsmoker	Exposed	—	1.51 (1.02–2.26)
Smoker	—	—	1.35 (0.70–2.63)
Smoker	Exposed	—	2.27 (1.64–3.13)
IUGR			
Nonsmoker	Exposed	—	1.08 (0.82–1.43)
Smoker	—	—	1.63 (1.06–2.53)
Smoker	Exposed	—	2.13 (1.70–2.67)

Number of nonsmokers not exposed to ETS = 3,235. Number of smokers not exposed to ETS = 222. Number of ETS-exposed smokers = 1,134.
[a]Adjusted for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, prepregnancy weight, alcohol consumption, and season. [b]ETS, 5 cig/day or more.

valid results; also, in our opinion the mother's tendency to deny smoking is strongest during advanced pregnancy. Therefore, the results based on smoking in the second trimester seem to be the best approximation of the impact of smoking during pregnancy, and we use them for this purpose in the present study.

LBW risk. Maternal smoking during pregnancy increased the relative risk of LBW considerably. Crude odds ratios (ORs) were 2.81 (CI, 2.21–3.71) for moderate and 4.95 (CI, 4.95–8.06) for heavy AS mothers. After adjustment for other covariates in logistic models, the values of adjusted ORs (AORs) were 1.83 (CI, 1.35–2.45) and 2.31 (CI, 1.34–4.08), respectively. We analyzed a possible influence of ETS exposure of nonsmoking women on LBW risk using logistic regression. Crude OR of LBW for infants of ETS-exposed mothers was 1.92 (CI, 1.32–2.77; $p < 0.0006$). The OR decreased after adjustment to 1.51 (CI, 1.02–2.26), but it remained significant ($p < 0.040$; Table 2).

Analyzing the combined effects of passive and active smoking during pregnancy on LBW risk, we again observed additive outcomes. Crude ORs and AORs for particular active smoking categories were higher for AS mothers simultaneously exposed to ETS (Table 4). The direct comparison of the LBW risk in the AS mothers without and with ETS exposure revealed quite convincing results. The AOR of ETS-exposed AS mothers was 2.02 (CI, 1.11–3.67).

We also tried to analyze the possible effects of smoking before (and during early) pregnancy on LBW risk, using the group of mothers who stopped smoking during early gestation. The crude and adjusted risks did not differ significantly from unity (data not shown). However, the sample size was not sufficient to make a valid consideration about the impact of smoking before pregnancy on LBW risk.

IUGR risk. Maternal smoking during pregnancy seriously increased the relative risk of IUGR. The crude ORs of IUGR were 2.41 (95% CI, 2.00–2.90) for moderate and 4.77 (95% CI, 3.29–6.90) for heavy AS mothers. AORs were 1.86 (95% CI, 1.51–2.30) and 3.25 (95% CI, 2.15–4.92), respectively. We then evaluated the relationship between ETS exposure of nonsmoking mothers and IUGR risk. The crude OR of IUGR for ETS-exposed mothers was 1.35 (95% CI, 1.04–1.74). This marginal association disappeared completely after adjustment for other associated variables (especially for maternal weight and height, parity, and parental education): AOR was then 1.08 (95% CI, 0.82–1.43; $p < 0.58$; Table 2). Examining the combined effects of active and passive smoking, the adjusted risks of IUGR in moderate AS mothers were higher for ETS-exposed mothers (Table 5). A valid comparison was not possible for heavy AS mothers because the subgroup of heavy AS_mothers without ETS exposure was too small. However, when both smoker groups are analyzed together, the additional effect of ETS is convincing. Exposure to passive smoking increased AOR of IUGR in AS mothers from 1.63 (CI, 1.06–2.53) for ETS-nonexposed AS mothers to 2.13 (CI, 1.70–2.67) for ETS-exposed AS mothers.

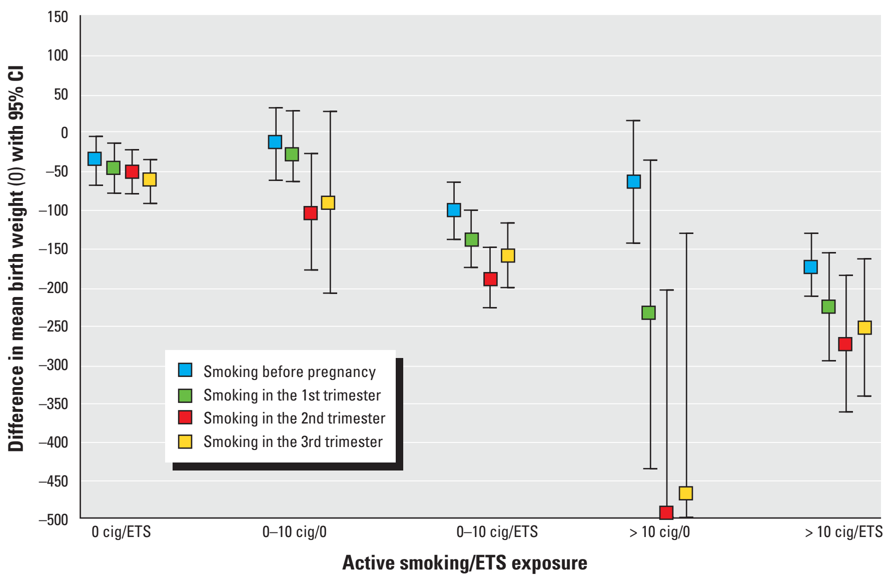

Figure 1. Simultaneous effects of active and passive maternal smoking on BW: mothers who stopped smoking in early gestation compared with those who continued. We adjusted mean decrements of BW for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, prepregnancy weight, alcohol consumption, and season. We based calculations for heavy AS mothers without ETS exposure (> 10 cig/0) on an insufficient number of cases.

Table 3. BW by active and passive smoking: women who stopped smoking after recognizing the pregnancy.

Maternal smoking	ETS exposure	No.	Adjusted[a] change (g)	95% CI	p-Value
Nonsmoker	—	3,188	0	—	—
	ETS[b]	1,049	–41	–5 to –77	0.019
Moderate[c]	—	276	+8	+46 to –31	0.7
	ETS	326	–69	–4 to –134	0.030
Heavy[d]	—	37	+47	+164 to –70	0.4
	ETS	115	–88	–17 to –159	0.012

[a]Adjusted for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, prepregnancy weight, alcohol consumption, and season. [b]ETS, 5 cig/day or more. [c]Moderate, 1–10 cig/day. [d]Heavy, > 10 cig/day.

Discussion

We found no association between self-reported ETS exposure of < 5 cig/day and BW or LBW in a pilot study (*20*). For this reason, we defined ETS operationally in the present study as exposure to ≥ 5 cig/day that were smoked by others in the mother's presence.

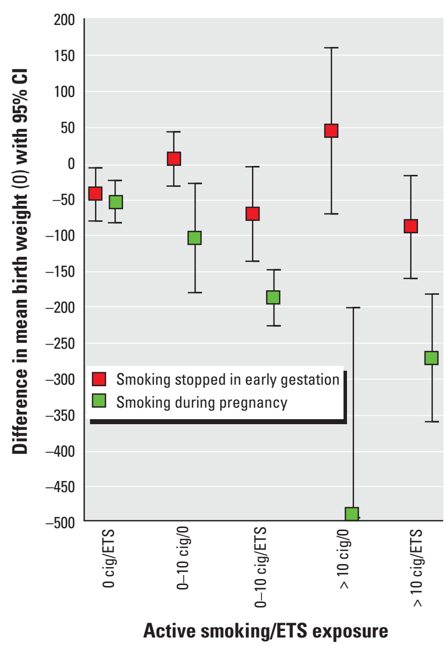

Figure 2. Simultaneous effects of active and passive maternal smoking on BW: calculation based on data about smoking habits during different gestational periods. We adjusted mean decrements of BW for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, prepregnancy weight, alcohol consumption, and season. We based calculations for heavy As mothers without ETS exposure (> 10 cig/0) on an insufficient number of cases.

We also found only insignificant differences between the reproductive effects of ETS in mothers who admitted relatively weak (e.g., 5–15 cig/day) and stronger (e.g., > 15 cig/day) passive exposure. This may reflects the fact that the self-reported quantitative estimates of ETS exposure were rather unreliable. Therefore, we evaluated ETS exposure as a dichotomous variable without classification to particular exposure groups.

The proportion of mothers who admitted smoking cigarettes at the start of pregnancy was relatively high (37%). About 30% of them stopped smoking after pregnancy was determined, another 25% gave up before the second trimester, and an additional 11% before the third trimester. We also observed some reduction in the daily number of cigarettes during pregnancy. The tendency to give up smoking during early or later gestation was much stronger in moderate (34% or 41%, respectively) than in heavy (13% or 14%) AS mothers; a similar conclusion was reached in other studies as well (*21*).

The impact of active smoking on BW was significant and dose–response related, as expected, considering current knowledge (*22,23*). In addition to smoking, the regression models included a spectrum of other covariates (see "Materials and Methods"). The results showed that BW was associated with many variables, such as maternal weight, ethnicity, parity, sex, and parental education. These factors are also related to smoking, and their effects explain a considerable part (about half) of the BW reduction that apparently seemed to be related to smoking. This follows from a comparison of the crude and adjusted BW decrements: The latter were invariably much lower (Table 1). Likewise, a relatively strong confounding of some associated covariates explained at least a part of the risk of adverse outcomes studied. This follows from the consistently higher values of crude ORs compared with AORs.

One important finding was that the relationship between BW and smoking grew stronger if the mother continued to smoke during pregnancy. Using data about the mother's smoking habits during different gestational phases, we showed that the smoking/BW association was stronger and BW decrements were higher during the later gestational phases (Table 1). An analysis of these data gives only supporting information about the impact of smoking during different gestational stages, however. For example, the results obtained from analyzing data about smoking habits during early gestation do not represent real effects of smoking during (and before) this period. Most smoking mothers from this period also continue smoking in later pregnancy, and the effect of this later exposure strengthens the BW/smoking relationship. Nevertheless, many mothers who were smoking during earlier gestational phases stopped smoking later in the pregnancy: This weakens the observed association between BW and smoking habits in the earlier periods compared with those based on smoking data from later gestation (Figure 1).

A direct evaluation of the effects of smoking on BW during different gestational phases was also possible using the present data. We analyzed the BW/smoking relationship in the subgroup of mothers who stopped smoking immediately after the pregnancy was recognized and compared the results with those of mothers who continued smoking until later gestational phases. The impact of smoking on BW before (and during early) pregnancy was only marginal and nonsignificant, although it suggested a dose relation (–23 g and –66 g, respectively). In contrast, when mothers continued to smoke even during the second trimester, mean BW was strongly reduced by about 150 g for moderate and 260 g for heavy AS mothers (Table 1). It seems that continuing to smoke during the third trimester did not considerably increase the already-existing effect of smoking. On the other hand, it follows from the above results that the effects of smoking on BW increase with the duration of smoking during pregnancy, at least until the end of the second trimester. This opinion supports the use of programs that encourage smoking cessation during pregnancy. The efficacy of such programs concurrently verifies the validity of the above-mentioned assumption (*24*).

In agreement with some other studies (*13,25–27*), we observed a significant relationship between ETS exposure and the BW of infants whose mothers declared themselves to be nonsmoking mothers. The mean adjusted BW decrement in ETS-exposed mothers was 53 g (Table 2). Moreover, ETS exposure seems to increase the impact of active smoking on BW. This additional effect of ETS exposure on BW reduction (when combined with maternal smoking) proved to be relatively strong during any gestational period, suggesting a causal relationship (Table 3, Figure 2). The final evidence brought the evaluation of BW decrement in infants of ETS-exposed AS mothers; the mean BW reduction was about 92 g compared with the weight of babies of AS mothers without ETS exposure.

One alternative explanation could be that mothers exposed to ETS are frequently living in smoking families or generally in a smoking milieu and may be more heavily exposed. This assumption was supported indirectly by our finding that the proportion of ETS-exposed mothers increases from 25% for nonsmoking mothers to 67% for mild and 85% for heavy AS mothers. It may be hypothesized that ETS-exposed mothers may smoke more cigarettes per day on average in any particular smoking class. To test this hypothesis, we compared the mean daily number of cigarettes reported by ETS-exposed and ETS-nonexposed mothers. In moderate AS mothers, the mean was 7.7 cig/day for ETS-exposed and 6.7 cig/day for ETS-nonexposed mothers. In heavy AS mothers, these averages were 19.3 cig/day and 17.6 cig/day, respectively. The differences were in the expected direction but are too small to explain the strong additional effects on BW apparently attributable to ETS exposure. On the other hand, the reported daily number of cigarettes that were smoked by others in the mother's presence differed considerably according to smoking

Table 4. The relative risk of LBW by active and passive smoking during pregnancy.

Maternal smoking	ETS exposure	No.	Crude OR (95% CI)	AOR[a] (95% CI)
Nonsmoker	—	3,713	1	1
	ETS[b]	1,797	1.79 (1.32–2.44)	1.43 (1.04–1.97)
Moderate[c]	—	210	1.40 (0.60–3.24)	1.01 (0.35–2.95)
	ETS	970	4.12 (3.04–5.57)	2.36 (1.80–3.65)
Heavy[d]	—	12[e]	36.6[e] (10.4–128.7)	19.2[e] (4.9–74.9)
	ETS	164	5.00 (2.86–8.78)	2.57 (1.37–4.80)

[a]Adjusted for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, pre-pregnancy weight, alcohol consumption, and season. [b]ETS = 5 cig/day or more. [c]Moderate = 1–10 cig/day. [d]Heavy = >10 cig/day. [e]The calculation was based on an insufficient number of cases.

Table 5. The relative risk of IUGR by active and passive smoking during pregnancy.

Maternal smoking	ETS exposure	No.	Crude OR (95% CI)	AOR[a] (95% CI)
Nonsmoker	—	3,713	1	1
	ETS[b]	1,797	1.37 (1.11–1.68)	1.19 (0.96–1.47)
Moderate[c]	—	210	1.77 (1.10–2.88)	1.39 (0.84–2.31)
	ETS	970	2.90 (2.34–3.59)	2.14 (1.67–2.73)
Heavy[d]	—	12[e]	12.7[e] (3.6–44.0)	7.1[e] (1.9–26.6)
	ETS	164	5.07 (3.41–7.54)	3.43 (2.19–5.36)

[a]Adjusted for maternal age, district, ethnicity, maternal education, paternal education, parity, sex, maternal height, pre-pregnancy weight, alcohol consumption, and season. [b]ETS = 5 cig/day or more. [c]Moderate = 1–10 cig/day. [d]Heavy = >10 cig/day. [e]The calculation was based on an insufficient number of cases.

habits. The self-reported ETS averages (for ETS-exposed mothers) were 11 cig/day for nonsmoking mothers, 14 cig/day for moderate AS mothers, and 23 cig/day for heavy AS mothers. This condition may partly explain the relatively strong additive effect of ETS exposure in AS mothers.

The impact of maternal smoking on the risk of LBW is well known (*22*); we also observed a strong and dose-related effect of active smoking during pregnancy in the present study. We found no effect of smoking before pregnancy on LBW risk, analyzing the subgroup of mothers who stopped smoking after pregnancy determination; however, the sample was too small to enable a valid consideration of this relationship.

A number of studies have analyzed the possible effect of passive smoking, each differing in many respects (*5,6,13,28–30*); the ETS exposure of the mothers was variously defined as smoking of the husband only, the estimated hours of exposure per day (e.g., > 2 hours), the number of cigarettes smoked in the presence of the mother, biomarker measurement (cotinine, nicotine), and the like. This circumstance aggravates the comparison of results. Nevertheless, most studies have shown a slightly elevated relative risk of LBW with ETS exposure, frequently nonsignificant. A National Cancer Institute report concluded that the results of an evaluation of 15 current studies were consistent with either a 1.4 or 1.5 times increased risk of small fetal size for ETS-exposed mothers or with no association at all (*31*). In the present study, we found a significantly increased risk of LBW in nonsmoking women who were exposed to ETS. The AOR of LBW in exposed women was 1.51 (CI, 1.02–2.26; Table 2). Moreover, our results supported the idea that exposure to ETS increases the effects of active smoking. The risk of delivering an LBW infant was higher for moderate AS mothers who were exposed simultaneously to ETS. The number of ETS-exposed heavy AS mothers was too small to make a valid comparison (Table 4). However, evaluating the AS mothers together, ETS exposure increased the LBW risk of AS mothers from 1.35 (CI, 0.94–2.01) to 2.27 (CI, 1.64–3.13; Table 2). This tendency seems to be true also for heavy AS mothers. This follows from a comparison of relative risk of LBW for all heavy AS mothers (AOR, 2.31;CI, 1.34–4.08) with that for the ETS-exposed fraction of heavy AS mothers from Table 4 (AOR, 2.57; CI, 1.37–4.80). The direct comparison of the LBW in babies of the AS mothers without and with ETS exposure shows that the LBW risk for infants of ETS-exposed AS mothers is two times higher.

The extent of the adverse effects of passive smoking on birth outcomes can be demonstrated also by calculating the LBW risk attributable to ETS exposure in nonsmoking mothers. According to present data, 37.2% of women smoked during pregnancy and 24.9% of nonsmoking mothers were exposed to ETS. The relative risk (AOR) of LBW in AS mothers was 1.94, and in ETS-exposed nonsmoking mothers the AOR was 1.51. We have extrapolated these conditions for the entire Czech population and estimated the attributable risk using a U.S. Environmental Protection Agency formula (*32*). Under these conditions, about 432 (8.3%) of the 5,224 infants born with LBW in the Czech Republic during 1999 were attributed to ETS exposure of nonsmoking mothers. Moreover, a slightly lower number of LBW babies should be additionally born to AS mothers because of their additional exposure to ETS.

We found a relatively weak but significant crude association of IUGR risk with passive smoking in the present study, but this association was completely explained by the effects of other factors, especially parity, parental education, and maternal height and weight. The AOR was close to unity (Table 2), in agreement with negative findings of others (*9,23,30,33*). On the other hand, a clear relationship between IUGR and ETS exposure was observed in many other well-designed studies (*13,22,34*). Recently, in another study we examined the possible influence of air pollution on IUGR risk using a similar sample and observed a significant association of IUGR risk with exposure during early gestation to fine particles and the carcinogenic fraction of polycyclic aromatic hydrocarbons (*19,35*). In addition, significantly increased levels of bulky DNA adducts were found in the placentas of ETS-exposed mothers and also in the placentas of IUGR infants (*36*). Considering these indirect indices, an adverse effect of ETS exposure on IUGR risk in nonsmoking mothers could be expected. Surprisingly, we observed no such effect. On the other hand, simultaneous exposure of AS mothers to ETS increased the original IUGR risk attributable to moderate active smoking; regrettably, a similar effect could not be observed directly in heavy AS mothers because of an insufficient sample size (Table 5). In contrast, ETS exposure distinctly increased the IUGR risk for AS mothers (Table 2). This additive effect is also shown for moderate AS mothers in Table 5 (data for heavy AS mothers are insufficient for analysis). This finding indicates that ETS exposure is not indifferent to IUGR risk. It may be a question of the ETS dose; as mentioned above, the mean ETS exposure (in cig/day) reported by AS mothers was much higher than that of nonsmoking mothers.

It has become obvious by now that not only active smoking but also ETS exposure during pregnancy may pose a reproductive risk. This assumption has also been supported in a growing number of studies based on biomarker data that allow more precise estimates of exposure compared with our self-reported estimates (*30*). The misclassification of exposure is an important consideration in epidemiologic studies such as this one. Studies dealing with the reliability of questionnaire responses mostly show that the qualitative information obtained is generally reliable but the quantitative information may not be (*37*). Thus, we are aware of the limited reliability of the questionnaire information used. Misclassification of an individual who is a smoker as a nonsmoker may weaken the apparent relative risk of smoking-related effects in AS mothers. Nonetheless, an analysis of such material may lead to valuable conclusions. As Perez-Stable et al. (*38*) suggested in a critical review of 11 studies, most smokers misclassified as nonsmokers were very light or occasional smokers. Moreover, although the present study is based on self-reported estimates of exposure, we did have indication of the reliability of the questionnaire data used: Cotinine levels in cord blood were analyzed in 161 cases from the study sample for purposes of a biomarker study (*39*). The cotinine data obtained were compared with questionnaire information. The distributions of cotinine levels in the blood of self-reported nonsmoking mothers differed significantly from those of AS mothers. They were very similar to the distributions found by other authors, as well (*40,41*). Cotinine levels > 5 ng among nonsmoking mothers were observed mostly in the subgroup of ETS-exposed nonsmokers. Based on an evaluation of the above results, the percentage of smoker/nonsmoker misclassification in the present study should be < 10%.

Conclusions

We can conclude that, in accordance with current knowledge, ETS exposure significantly reduced the BW of infants delivered by nonsmoking women. The present study also showed that ETS exposure increases the adverse effects of active smoking. Thus, ETS contributed to BW reduction in babies of AS mothers. The exposure to ETS increased the risk of LBW infants not only for nonsmoking but also for AS mothers. We found a similar relationship between IUGR risk and ETS exposure only as an additional risk in AS mothers. The adjusted relative risk of IUGR in ETS-exposed nonsmoking mothers was not different from unity.

The impact of active smoking during pregnancy on BW was much stronger than the impact of similar levels of smoking before (and during early) pregnancy. It appears that the impact of active and/or passive smoking on fetal growth increases with the duration of exposure during pregnancy. This observation shows the usefulness of programs encouraging smoking cessation during pregnancy. The presented results support the presumption that ETS exposure during pregnancy represents an important factor that can endanger fetal development and increase the prevalence of adverse birth outcomes. Our results suggest that about 8% of all neonates with LBW born in the Czech Republic may be attributed to ETS exposure of nonsmoking mothers. Another portion of LBW births, although slightly smaller, may be due to the ETS exposure of smoking women.

References and Notes

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